

## REMARKS

Claims 29-40 and 70-77 are now pending. The Applicants respectfully request the Examiner to reconsider the rejections in view of amendments to the claims now presented and the following remarks.

### Claim Objections

The Applicants have addressed the objections to the claims as recommended. The Examiner is respectfully requested to withdraw all outstanding objections to the now pending claims.

### Rejections under 35 USC §112, paragraph 1, and §132

A. The Applicants now amend the claims to remove all references to “non-modified” to render the rejections moot as to the issue of new matter.

B. The Applicants now remove the term “or derivative thereof” from the claims to render the 112 paragraph 1 rejection moot since it is not a necessary term in view of the written description of the invention.<sup>1</sup>

C. In view of the Examiner’s acknowledgment that the Applicants instant specification provides enabling support under 35 USC §112 for increasing immune response or activating dendritic cells comprising administering a composition comprising a polynucleotide encoding an antigen, the Applicants have amended the claims accordingly.<sup>2</sup>

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<sup>1</sup> The Applicants respectfully highlight the written description, for example, at page 45 of the specification, lines 2-18.

<sup>2</sup> Examples of polynucleotides are listed at page 48 of the specification. Compositions comprise, for example, at least one gene expressing the antigen and a gene expressing the molecule that can activate dendritic cells or other antigen presenting cells and thus can serve as adjuvant (p. 48 lines 24-28). The examples of adjuvants are presented on p. 48 line 28 to p. 50, line 8). Importantly, the genes driven by NFkB or CMV promoter are preferred. (It important to know also that CMV promoter ALSO contains the NFkB element). At the same time constructs under SV-40 promoter it activated by the the formulation to my less extent, while genes under AP-1-sensitive cassette are not activated (see Example 62) as well as p. 49, line 6 to p. 50 line 8.

Accordingly, the Applicants respectfully request the Examiner to withdraw all rejections under 35 USC §112, paragraph 1, and §132.

#### **Rejections under 35 USC §112, paragraph 2**

The Examiner has alleged that the subject matter of the claims is indefinite under 35 USC § 112 ¶2.

The Applicants have amended the claims to address all issues raised by the Examiner. The rejections concerning the “non-modified” and “or derivative thereof” language are now moot in view of the amendments to the claims presented herewith. Claims 30, 33, 35, 38, and 71 are amended to correct antecedent basis. Claim 77 is amended to particularly point out and distinctly claim the subject matter the Applicants regard as the invention.

The Applicants therefore respectfully request the Examiner to withdraw the rejections under 35 USC §112, paragraph 2.

#### **Rejections under 35 USC §102(e)**

The Applicants respectfully remind the Examiner that Anticipation under 35 USC §102(e) requires that the claimed subject matter, *per se*, i.e., all express limitations, must be found in a single disclosure filed by another before the Applicants application for patent.

The Applicants have now amended the claims to require the administration of a composition comprising at least one polynucleotide wherein an antigen *and* an adjuvant are expressed from the at least one polynucleotide. The Examiner is particularly referred to page 48, line 24, *et seq.*, of the instant Specification where the Applicants teach that more than one polynucleotide is preferably expressed. Specifically preferred is at least one polynucleotide expressing an antigen and at least one polynucleotide expressing an adjuvant molecule. Further described in the written description is the fact that polynucleotides which comprise the CMV promoter or NF-κB-sensitive element cassette are considerably more efficacious in formulations of the present invention. See, page 49, lines 6-28, for example.

The Manthorpe '358 published application is drawn toward the use of salts, in particular sodium and potassium salts of phosphate, in aqueous solution, and auxiliary agents, in particular detergents and surfactants, in pharmaceutical compositions and methods useful for direct

polynucleotide-based polypeptide delivery into the cells of vertebrates; however, compositions comprising a polynucleotide which encodes an antigen and a polynucleotide which encodes an adjuvant are not contemplated.

The Kabanov, *et al.*, references cited by the Examiner, i.e., the '406 and '459 patents, even if they were properly cited as prior art under 35 USC §102(e), cannot as a matter of law anticipate the claimed invention because compositions comprising a polynucleotide which encodes an antigen and a polynucleotide which encodes an adjuvant are not contemplated. Accordingly, 102(f) is a moot issue.

Accordingly, the Applicants respectfully request the Examiner to withdraw all rejections under 35 USC §102.

### **Rejections under 35 USC §103**

The Examiner has alleged that the subject matter of claims 29, 31-32, 34, 36-37, 39-40, 69-70, 72, and 74-77 is obvious under 35 USC §103 over Raz, *et al.*, '940, in view of Kabanov, *et al.*, '611. The Examiner has further alleged that the subject matter of these same claims is obvious over Carson, *et al.*, '877, again in view of Kabanov, *et al.*, '611. Still further, the Examiner has alleged that the subject matter is obvious over Raz, *et al.*, '940, or Carson, *et al.*, '877 and Kabanov, *et al.*, '611, further in view of Kabanov, *et al.*, '438.

The Applicants respectfully remind the Examiner that motivation to combine the references must be present to solve the same problem, i.e., to induce activation of dendritic cells. Moreover, most importantly with regard to the facts of the claims presented, all the limitations of the instant claims must be found within the prior art references to render the claimed subject matter *prima facie* obvious.

The nucleic acid contemplated by Raz '940 is not equivalent or comparable to an adjuvant or antigen defined within the scope of the instant written description and presented claims.<sup>3</sup> Moreover, the '940 disclosure does not contemplate, suggest, or describe the critical

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<sup>3</sup> Although Raz, *et al.*, contemplate the administration of an oligonucleotide sequence, column 4, line 34, for example, the entire contemplated entity is composed of about 8 nucleotides.

formulation. i.e., polyoxyethylene-polyoxypropylene block co-polymers. The Kabanov '611 disclosure particularly teaches and stresses the advantages of polycationic polyether block copolymers compositions to increase the ability of nucleic acids to cross cell membranes; however, the '611 disclosure does not contemplate, suggest, or describe any method of inducing the activation of dendritic cells *or* any method of modulating an immune response. Both Carson'877 *and* Kabanov '611 stress and teach toward *cationic entities* to merely effect of nucleic acid delivery. Kabanov '438 does not teach formulations for the administration of nucleic acids *or* for the activation of dendritic cells.

Importantly, however, nowhere in any of the references cited are compositions contemplated which comprise both a polynucleotide which encodes an antigen and a polynucleotide which encodes an adjuvant (the same or separate nucleic acids) as defined by the claims now presented.

Accordingly, the Applicants respectfully request the Examiner to withdraw the rejections under 35 USC §103.

#### **Obviousness-Type Double Patenting Rejection**

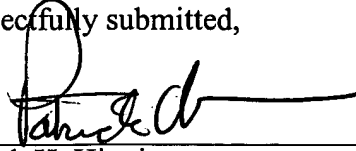
The Applicants respectfully submit that the double patenting issues are each moot in view of amendments to the claims presented herewith. The Applicants, in any event, elect to defer resolution of this issue until the final scope of the pending claims is determined. The Applicants' indeed, however continue to acknowledge their willingness to execute a terminal disclaimer under 37 CFR §1.321(c) if necessary.

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For all the foregoing reasons, the Applicants submit that Claims 29-40 and 70-77 are in condition for allowance. Early action toward this end is courteously solicited. *The Examiner is kindly encouraged to telephone the undersigned in order to expedite any detail of the prosecution.*

The Commissioner is authorized to charge any deficiency or credit any overpayment in connection herewith to Deposit Account No. 13-2165.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Patrick H. Higgins", written over a horizontal line.

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